CLAIMS

What is claimed is:

1. A library of cultured eucaryotic cells made by a process comprising the steps of:

a) treating a first group of cells to stably integrate a first vector that mediates the splicing of a foreign exon internal to a cellular transcript;

b) treating a second group of cells to stably integrate a second vector that mediates the splicing of a foreign exon 5′ to an exon of a cellular transcript; and

c) selecting for transduced cells that express the products encoded by the foreign exons.

2. The library of claim 1 wherein said treating is transfection.

3. The library of claim 1 wherein said treating is by infection.

4. The library of claim 1 wherein said treating is by retrotransposition.

5. The library of any one of claims 1 through 4 wherein said cells are animal cells.

6. The library of claim 5 wherein said animal is mammalian.

7. The library of claim 6 wherein said cells are rodent cells.

8. The use of a mutated cell from a library according to claim 6 to generate a non-human transgenic animal.

9. A vector for replacing the 3′ end of an animal cell transcript with a foreign exon, comprising:

a) a selectable marker;

b) a splice acceptor site operatively positioned 5′ to the initiation codon of said selectable marker;

c) a polyadenylation site operatively positioned 3′ to said selectable marker;

d) said vector not comprising a promoter element operatively positioned 5′ of the coding region of said selectable marker; and

e) said vector not comprising a splice donor sequence operatively positioned between the 3′ end of the coding region of said selectable marker and said polyadenylation site.

10. A vector for inserting foreign mutagenic polynucleotide sequence internal to animal cell transcripts, comprising:

a) a foreign exon;

b) a splice acceptor sequence operatively positioned 5′ to the foreign exon;

c) a splice donor site operatively positioned 3′ to said foreign exon;

d) a sequence comprising a nested set of stop codons in each of the three reading frames located between the 3′ end of said foreign exon and said splice donor site;

e) said vector not comprising a polyadenylation site operatively positioned 3′ to said foreign exon; and

f) said vector not comprising a promoter element operatively positioned 5′ to the coding region of said foreign exon.

11. A vector for attaching a foreign exon upstream from the 3′ end of an animal cell transcript, comprising:

a) a selectable marker;

b) a promoter element operatively positioned 5′ to said selectable marker;

c) a splice donor site operatively positioned 3′ to said selectable marker; and

d) said vector not comprising a transcription terminator or polyadenylation site operatively positioned relative to the coding region of said selectable marker; and

e) said vector not comprising a splice acceptor site operatively positioned between said promoter element and the initiation codon of said selectable marker.

12. The vector of claim 11 wherein said vector additionally comprises a foreign mutagenic polynucleotide sequence located upstream from said promoter.

13. The vector of claim 12 wherein said vector additionally comprises a splice acceptor operatively positioned upstream from said foreign mutagenic polynucleotide sequence.

14. The vector of claim 13 wherein said foreign mutagenic polynucleotide sequence comprises a polyadenylation site.

15. The vector of claim 14, wherein said foreign mutagenic polynucleotide sequence additionally comprises stop codons in all three reading frames.

16. The vector of claim 12 in which a first recombinase recognition sequence is present upstream from said promoter and a second recombinase recognition sequence is present downstream from said promoter.

17. The vector of any one of claims 9, 10, or 11 wherein said vector is a viral vector.

18. The vector of claim 17 wherein said viral vector is a retroviral vector.

19. The use of a vector according to claim 9 to produce a library of mutated animal cells.

20. The use of a vector according to claim 10 to produce mutated animal cells.

21. The use of a vector according to claim 11 to produce mutated animal cells.

22. The use of a vector according to claim 11 to effect homologous recombination in an animal cell.

23. A stably transduced animal cell that incorporates a vector according to claim 16.

24. A method of deleting a region of vector DNA from a cell according to claim 23, comprising:

a) providing a recombinase activity to the cell; and

b) selecting for cells that lack the desired region of vector DNA.

25. A method of adding a region of DNA to a cell according to claim 23, comprising:

a) introducing the DNA to be added into the cell;

a) providing a recombinase activity to the cell; and

b) selecting for cells that incorporate the added DNA.

26. A method of effecting the inducible expression of a desired gene, comprising:

a) providing a cell according to claim 23 with a recombinase gene that is controlled by an inducible promoter; and

b) inducing said inducible promoter.

27. A method of gene discovery comprising:

a) adding a foreign polynucleotide to a population of target cells such that the foreign

polynucleotide is inserted throughout the genomes of the target cells; and

b) activating control elements encoded by the foreign polynucleotides that activate or repress the expression of target cell genes that flank the integrated foreign polynucleotides, and identifying the regions of the target cell genome into which the foreign polynucleotides have integrated.

28. A library of cultured animal cells that stably integrate a vector according to any one of claims 10 or 11.